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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,257	02/14/2002	Chih-Pin Liu	1954-313	5061

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
08/28/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/074,257	LIU ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,11-16,23-25,32-34,53 and 54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 11-16, 23-25, 32-34 and 53-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application claims the benefit of the filing date of provisional application 60/268,714.

Claims 5-10, 17-22, 26-31 and 35-52 have been canceled.

Claims 1-4, 11-16, 23-25, 32-34 and 53-54 are currently pending.

In view of the declaration of Chih-Pin-Liu and the response filed May 3, 2007, the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-4, 12, 13, 15, 23, 24, 32-34, 53 and 54 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tisch et al. (J. Immunol. [1999] 163:1178-1187; cited on form PTO-1449 filed June 18, 2002) as evidenced by Wong et al (Diabetes [2005] 54: 2032-2040; U on form PTO-892), both of record, in view of Crawford et al. (Immunity [1998] 8:675-682; cited on form PTO-1449 filed June 18, 2002) and U.S. Patent No. 5,635,363 to Altman et al. (A on form PTO-892), both newly cited).

It was previously stated: "The claims are broadly drawn to MHC class II murine I-Ag7 or human HLA-DQ complexes comprising a GAD peptide selected from SEQ ID NOs: 1-13. Tisch teaches the administration of GAD peptides including SEQ ID NO: 2, 3 and 4 to non-obese diabetic (NOD) mice. Tisch teaches that each of the peptides prophylactically inhibited the development of diabetes in the mice and that the peptide comprising SEQ ID NO: 3 assisted in the prevention of the progression of insulitis in NOD mice exhibiting autoimmunity (Abstract in particular). While Tisch does not disclose the MHC haplotype of the NOD mice, Wong et al evidences that NOD mice express I-A^{g7} (Abstract in particular).

Tisch does not teach isolated complexes of MHC class II with GAD peptides.

Crawford teaches the making of recombinant MHC class II molecules with antigenic peptides attached to the beta chain (see entire reference). Crawford teaches that theses molecules are soluble (page 677, column 2 in particular), and therefore the molecules lack at least part of the alpha and beta

transmembrane domains. Crawford teaches the multimerization of the MHC/peptide moieties by biotinylation of the soluble MHC/peptide constructs (page 680, column 1 in particular). Crawford further teaches the attachment of an effector molecule that is a detectable fluorescent label (page 680, column 1 in particular) [claims 33,34]. Crawford teaches that the multimeric complexes bind specifically to normal T cells and to T cell hybridomas.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to construct soluble recombinant versions of the MHC class II/GAD peptide combinations taught by Tisch using the method of Crawford. One would have been motivated to combine the teachings with a reasonable expectation of success by the teachings of Tisch that the GAD peptides were effective in inducing regulatory Th2 cells and by the teachings of Crawford the multimeric construct "reagents have obvious usefulness in identifying and tracking antigen-specific T cells during normal or pathogenic immune responses" page 679, column 2 in particular). One would have been further motivated to make such complexes for therapeutic purposes by the teachings of the '363 patent, which teaches that specific antigen/receptor complexes are useful for targeting very specific subsets of T cells and treating a variety of diseases, including diabetes (column 11, lines 39-65 in particular)."

Applicant's arguments and the declaration of Chih-Pin-Liu filed May 3, 2007 have been fully considered but they are not persuasive.

The declaration contends that the claimed invention should not be considered obvious over the combination of references because the inventor applied for a grant on the claimed subject matter and received commentary from the grant reviewers expressing doubt over the proposed approach, which is the same as the method described in the instant specification. This argument is not convincing however, because the claims are drawn to a complex, not a particular method. If the same complex can be made by a different method it still reads upon the claimed complex, irrespective of the method. Furthermore, Applicant did not indicate whether the negative opinion was a majority opinion resulting in the denial of the grant request, or if the opinion was simply a concern raised by a reviewer in a grant that was nevertheless funded.

In the response, Applicant argues that the claimed invention could not be considered obvious over the combination of references because Tisch does not teach complexes and the '363 patent was not discussed. The arguments are not convincing. First of all, the office action never stated that Tisch individually taught complexes. The Office Action clearly stated, "Tisch does not teach isolated complexes of MHC class II with GAD peptides." However, Tisch does clearly teach the use of MHC class II binding peptides for the prophylactic treatment of mice. Crawford teaches a method for making a complex of MHC class II binding peptides with MHC class II molecules. By practicing the COMBINATION of Tisch with Crawford, the artisan would be led to make MHC class II molecules complexed with GAD peptides. Despite Applicant's contention that the '363 patent is not discussed, it is clear in the previous Office Action that the '363 was discussed in that it would provide the artisan with

motivation to make the combination of Tisch and Crawford, in that it "teaches that specific antigen/receptor complexes are useful for targeting very specific subsets of T cells and treating a variety of diseases, including diabetes (column 11, lines 39-65 in particular)." Contrary to Applicant's assertion, none of the references have to individually teach or suggest MHC class II/GAD complexes.

2. Claims 14, 16 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tisch et al. (J. Immunol. [1999] 163:1178-1187; cited on form PTO-1449 filed June 18, 2002) as evidenced by Wong et al (Diabetes [2005] 54: 2032-2040; U on form PTO-892), both of record, in view of Crawford et al. (Immunity [1998] 8:675-682; cited on form PTO-1449 filed June 18, 2002) and U.S. Patent No. 5,635363 to Altman et al. (A on form PTO-892), both newly cited as applied to claims 1, 2 and 23 above, and further in view of U.S. Patent No. 5,595,881 to Kendrick et al (patent date May, 15, 2001, filed October 29, 1997; B on form PTO-892 of record).

It was previously stated: "Tisch and Crawford have been discussed supra.
The combined references do not teach oligohistidine tags.
The '881 patent further teaches that recombinantly produced soluble MHC molecules can be engineered to comprises a tail or "tag," such as oligohistidine that can be used for purification [claims 9 and 10] (column 9, line 39 to column 10, line 36 in particular).
It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Tisch and Crawford with the teachings of the '881 patent to create MHC class II complexes comprising GAD 65 peptide antigens and bearing an oligohistidine tag. The artisan would have been motivated to combine the teachings with a reasonable expectation of success to create to create soluble single-chain MHC class II molecules covalently bound to GAD 65 antigenic peptides by combining the teachings Tisch and Crawford as set forth supra and tagging the molecules by incorporating an oligohistidine tail as taught by the '881 patent in order to simplify the purification of the recombinantly produced molecules from culture medium."

Applicant's arguments regarding the '881 patent amount to a contention that the '881 patent also does not provide a working model of Applicant's invention. However, the combination of references do not need to physically present Applicant's invention, but must provide a reasonable expectation of success to perform the claimed invention when the teachings are combined.

Conclusion

3. No claim is allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
November 13, 2006

David A Saunders

DAVID A. SAUNDERS
PRIMARY EXAMINER